DOCKET NO.: DIBIS-0002US.P5 (Counsel Docket No. 10468) **PATENT**

IN THE CLAIMS:

1-12. (cancelled)

13. (currently amended) A forensic method of mitochondrial DNA analysis comprising the steps of:

obtaining a database comprising a plurality of known molecular masses of restriction fragments produced by restriction enzymes from a segment of mitochondrial DNA from a plurality of subjects;

amplifying said segment from test mitochondrial DNA obtained from a test subject to obtain a test amplification product;

digesting ~~an~~ said test amplification product ~~of a first mitochondrial DNA identifying amplicon~~ with said restriction enzymes to produce ~~a plurality~~ test ~~of~~ restriction fragments;

determining ~~first~~ the molecular masses of said test restriction fragments by mass spectrometry; and

comparing ~~the first~~ said molecular masses of said test restriction fragments with ~~second molecular masses of restriction fragments of a second mitochondrial DNA identifying amplicon obtained with the restriction enzymes~~ said plurality of known molecular masses, thereby reaching a forensic conclusion.

14. Cancelled.

15. (original) A forensic method of claim 13 wherein the restriction enzymes are any combination of *Rsa*I , *Hpa*II, *Hpy*CH4IV, *Pac*I, and *Eae*I.

16. (currently amended) A forensic method of claim 14 wherein ~~the subject is an animal~~ said subjects are animals.

17. (currently amended) A forensic method of claim 16 wherein ~~the animal is a human~~ said animals are humans.

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18. (currently amended) A forensic method of claim 14 wherein ~~the subject is a nonhuman eukaryotic organism, a fungus, a parasite, or a protozoan~~ said subjects are nonhuman eukaryotic organisms, fungi, parasites or protozoa.

19. (currently amended) A forensic method of claim 1 wherein ~~the mitochondrial DNA identifying amplicon~~ said segment comprises a portion of a hypervariable region of mitochondrial DNA.

20. (original) A forensic method of claim 19 wherein the hypervariable region comprises HV1 or HV2.

21. (cancelled)

22. (currently amended) A method of characterizing ~~the~~ heteroplasmy of a segment ~~sample~~ of mitochondrial DNA of an individual comprising the steps of:

amplifying said segment of mitochondrial DNA with a pair of primers to obtain a plurality of test amplification products corresponding to said segment;

determining ~~the~~ molecular masses of ~~a~~ said plurality of amplification products ~~of the mitochondrial DNA~~; and

~~determining the relative quantities of the plurality of amplification products,~~ determining base compositions of said plurality of amplification products thereby characterizing ~~the~~ said heteroplasmy.

23. (currently amended) A method of claim 22 ~~wherein~~ further comprising obtaining a plurality of samples of mitochondrial DNA ~~are obtained~~ from ~~an~~ said individual at different points of the lifetime of the individual, whereby the characterization of heteroplasmy indicates the rate of naturally occurring mutations in mitochondrial DNA.

24. (original) A method of claim 23 further comprising correlating the rate of naturally occurring mutations in mitochondrial DNA with the rate of onset of mitochondrial disease in a plurality of individuals affected by mitochondrial disease, wherein the correlation provides a means for predicting the rate of onset of mitochondrial disease.

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25. (original) The method of claim 24 wherein the mitochondrial disease is Alpers Disease, Barth syndrome, Beta-oxidation Defects, Carnitine-Acyl-Carnitine Deficiency, Carnitine Deficiency , Co-Enzyme Q10 Deficiency, Complex I Deficiency, Complex II Deficiency, Complex III Deficiency , Complex IV Deficiency, Complex V Deficiency, COX Deficiency, CPEO, CPT I Deficiency, CPT II Deficiency, Glutaric Aciduria Type II, KSS, Lactic Acidosis, LCAD, LCHAD, Leigh Disease or Syndrome, LHON, Lethal Infantile Cardiomyopathy, Luft Disease, MAD, MCA, MELAS, MERRF, Mitochondrial Cytopathy, Mitochondrial DNA Depletion, Mitochondrial Encephalopathy, Mitochondrial Myopathy, MNGIE, NARP, Pearson Syndrome, Pyruvate Carboxylase Deficiency, Pyruvate Dehydrogenase Deficiency, Respiratory Chain, SCAD, SCHAD, or VLCAD.

26-28. (Cancelled).

29. (new) The method of claim 22 wherein said molecular masses are determined by mass spectrometry.

30. (new) The method of claim 29 wherein said mass spectrometry is electrospray Fourier transform ion cyclotron resonance mass spectrometry or electrospray time-of-flight mass spectrometry.

31. (new) The method of claim 29 further comprising determining the relative amounts of each member of said plurality of amplification products from the abundance of mass spectral peaks corresponding to members of said plurality of amplification products.

32. (new) The method of claim 13 wherein said forensic conclusion comprises identification of a subject from whom said test mitochondrial DNA is obtained by comparing said molecular masses of said test restriction fragments with said plurality of known molecular masses.

33. (new) The method of claim 13 wherein said forensic conclusion comprises tracking of the geographic location of a subject from whom said test mitochondrial DNA is obtained by analyzing a plurality of test mitochondrial DNA samples according to the method of claim 13 wherein said plurality of test mitochondrial DNA samples is obtained from a plurality of geographic locations and time points.

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34. (new) A method of mitochondrial DNA analysis comprising the steps of:

a) obtaining a database comprising a plurality of known base compositions of restriction fragments produced by restriction enzymes from a segment of mitochondrial DNA from a plurality of subjects;

b) amplifying said segment from test mitochondrial DNA obtained from a test subject to obtain a test amplification product;

c) digesting said test amplification product with said restriction enzymes to produce test restriction fragments;

d) determining molecular masses of said test restriction fragments;

e) calculating base compositions of said test restriction fragments from said molecular masses determined in step d); and

f) comparing said base compositions of said test restriction fragments with said plurality of known base compositions, thereby reaching a forensic conclusion.

35. (new) The forensic method of claim 34 wherein the restriction enzymes are any combination of *Rsa*I , *Hpa*II, *Hpy*CH4IV, *Pac*I, and *Eae*I.

36. (new) The method of claim 34 wherein said subjects are animals.

37. (new) The method of claim 36 wherein said animals are humans.

38. (new) The method of claim 34 wherein said subjects are nonhuman eukaryotic organisms, fungi, parasites, or a protozoa.

39. (new) The method of claim 34 wherein said standard segment comprises at least a portion of a hypervariable region of mitochondrial DNA.

40. (new) The method of claim 39 wherein the hypervariable region comprises HV1 or HV2.

41. (new) The method of claim 34 wherein said step of determining molecular masses of step d) is performed by mass spectrometry.

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42. (new) The method of claim 41 wherein said mass spectrometry is electrospray Fourier transform ion cyclotron resonance mass spectrometry or electrospray time-of-flight mass spectrometry.

43. (new) The method of claim 34 wherein said forensic conclusion comprises identification of a subject from whom said test mitochondrial DNA is obtained.

44. (new) The method of claim 34 wherein said forensic conclusion comprises tracking of the geographic location of a subject from whom said test mitochondrial DNA is obtained.

45. (new) The method of claim 22 wherein said heteroplasmy is length heteroplasmy or single nucleotide polymorphism heteroplasmy.

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